# The *Krebs Cycle* as a Model for Connecting Biological Themes

I. Overview of the Krebs Cycle

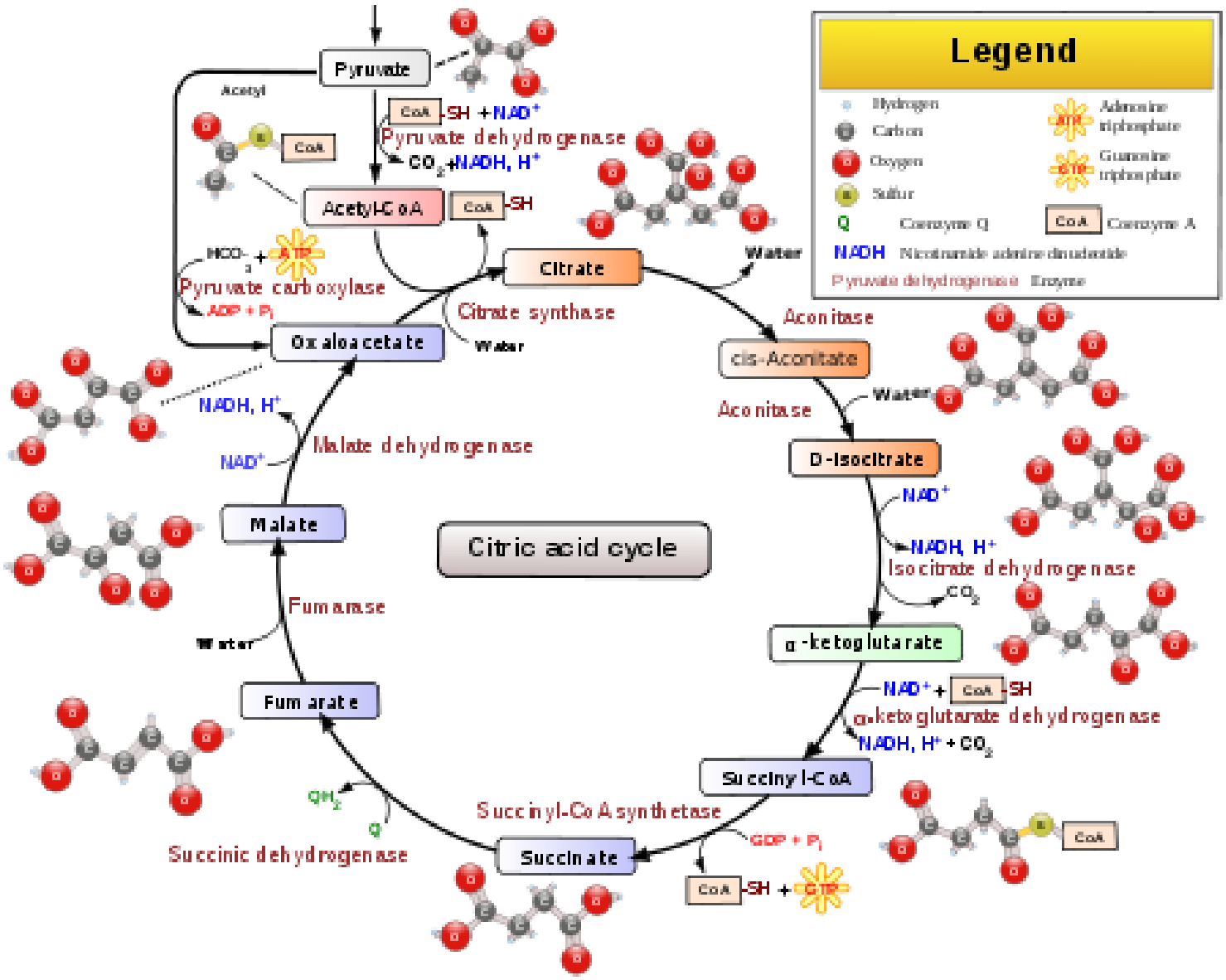
Function: Create high-energy molecules *directly* and *indirectly* by breaking down carbon compounds (**carbohydrates**/lipids/proteins).

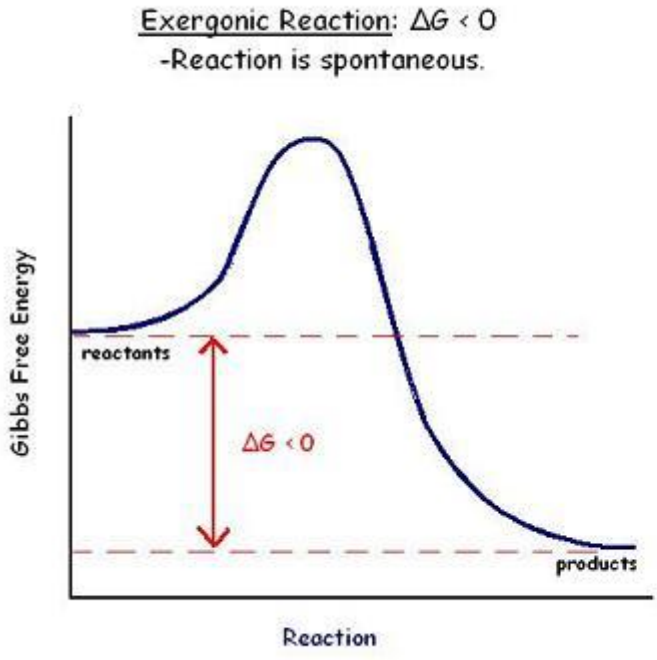
Description: A **cyclic** pathway of about 8 steps. Each step is performed by a unique **enzyme**. In Eukaryotes, the pathway occurs in the mitochondria, separated from all other cytoplasmic reactions. In prokaryotes, the pathway occurs in the cytoplasm amidst many other reactions, but it's thought to be localized in particular regions. Nearly the **same enzymes** are used for a vast variety of organisms.

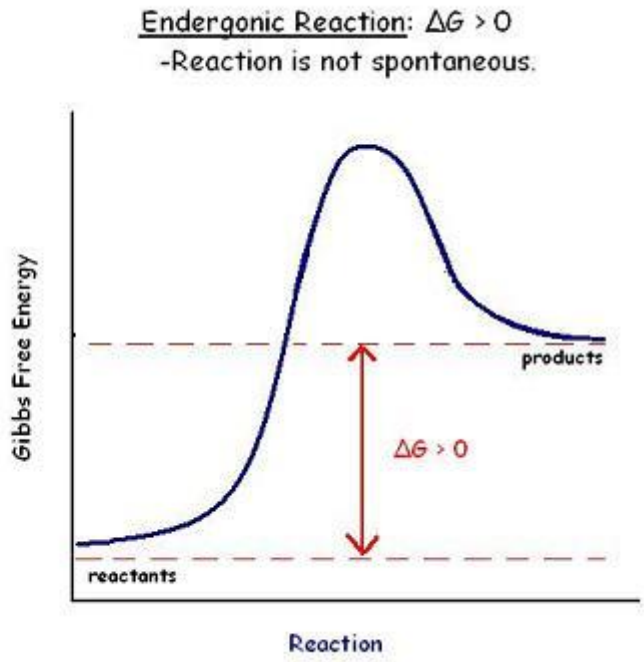
Some time ago, scientists had a lot of time on their hands and figured out approximately how much free energy is either released (-) or required (+) during each step. These numbers are provided in the table below.

Table 1: Free energy changes for steps in the Krebs cycle

| Reaction | Enzyme | $\Delta G^{\circ\prime}$ (kJ · mol$^{-1}$) |
|---|---|---|
| 1 | Citrate synthase | −31.5 |
| 2 | Aconitase | ~5 |
| 3 | Isocitrate dehydrogenase | −21 |
| 4 | α-Ketoglutarate dehydrogenase multienzyme complex | −33 |
| 5 | Succinyl-CoA synthetase | −2.1 |
| 6 | Succinate dehydrogenase | +6 |
| 7 | Fumarase | −3.4 |
| 8 | Malate dehydrogenase | +29.7 |


Legend
Hydrogen
Carbon
Oxygen
Sulfur
Adenosine triphosphate
Guanosine triphosphate
Coenzyme Q
Coenzyme A
NADH Nicotinamide adenine dinucleotide
Pyruvate dehydrogenase Enzyme
Pyruvate
Acetyl
CoA-SH + NAD+
Pyruvate dehydrogenase
CO2 + NADH, H+
Acetyl-CoA
CoA-SH
HCO3- + ATP
Pyruvate carboxylase
ADP + Pi
Citrate
Water
Citrate synthase
Oxaloacetate
Water
Aconitase
cis-Aconitate
Water
Aconitase
D-Isocitrate
NAD+
NADH, H+
Isocitrate dehydrogenase
CO2
α-ketoglutarate
NAD+ + CoA-SH
α-ketoglutarate dehydrogenase
NADH, H+ + CO2
Succinyl-CoA
Succinyl-CoA synthetase
GDP + Pi
CoA-SH + GTP
Succinate
QH2
Q
Succinic dehydrogenase
Fumarate
Water
Fumarase
Malate
NADH, H+
NAD+
Malate dehydrogenase
Citric acid cycle




II. Modeling Reactions: Note the reaction energy requirements for each step of the Kreb's Cycle.

III. Readings

*Lateral Gene Transfer as a Source of Genetic Variation*

Far beyond the traditional and well-researched origin of new genes by mutations in duplicated copies, genomics has revealed an array of previously unexpected sources of genetic novelty (Kaessmann 2010). One pathway that has often been ignored in discussions of the origin of novel genes is functional transfer from the cytoplasmic organelles or their endosymbiotic precursors (Timmis et al. 2004). Mitochondria and plastids were once free-living prokaryotes that evolved into extant cytoplasmic organelles during endosymbiotic evolution (Margulis 1970). The genomes of these organelles are now greatly reduced in size compared with those of their free-living ancestors. In large part, this is due to wholesale relocation of genes from the prokaryote ancestors to the nuclear genome followed by their subsequent deletion from the organelle genomes (Timmis et al. 2004;Kleine et al. 2009). The constant ingress of organelle DNA to the nucleus (Huang et al. 2003; Stegemann et al. 2003; Sheppard et al. 2008) has contributed a great diversity of new genetic material for evolutionary tinkering and it is a major past and present pathway for the generation of new genes (Timmis et al. 2004).

In the majority of cases, organelle DNA transferred to the nucleus is nonfunctional and its sequence may decay rapidly and/or it may be eliminated from the nuclear genome (Matsuo et al. 2005; Sheppard and Timmis 2009). In rare cases, however, gene transfer is accompanied or followed by the acquisition of a nuclear promoter and a polyadenylation signal leading to nuclear activation. Many proteins encoded by such genes retain their original function and are imported back into the organelle if they also acquire an appropriate transit peptide. Others may adopt novel roles that are unrelated to those they previously carried out (Martin et al. 2002). Smaller fragments of organelle DNA can also add to the complexity of nuclear genomes by contributing exonic or intronic sequences to existing nuclear genes (Noutsos et al. 2007).

Explain how each of the 4 Big Ideas below is demonstrated by citing at least 1 piece of evidence from the materials provided.

- Organisms **share** many **conserved core processes and features** that evolved and are widely distributed among organisms today [Big Idea 1]
- All living systems **require constant input of free energy** [Big Idea 2]
- Biological systems have **multiple processes** that increase genetic variation [Big Idea 3]
- **Variation in molecular classes** provide cells with a **wider range of function** [Big Idea 4]